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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/705,245	CHEN ET AL.	
	Examiner	Art Unit	
	Stephen Kapushoc	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,8-12,20 and 22-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,8-12,20 and 22-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 7-20, 22-25 are pending.

Claims 7, and 13-19 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention. Claim 7 is drawn to a non-elected drug and non-elected allele; Claims 13-19 are drawn to a non-elected invention.

Claims 1, 8-12, 20 and 22-25 are examined on the merits.

Please note: The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This Office Action is in reply to Applicants' correspondence of 12/7/2007.

Applicants' remarks, amendments, and Declaration have been fully and carefully considered but are not found to be sufficient to put this application in condition for allowance. This Office Action reinstates rejections and presents new grounds of rejection that are not necessitated by the amendments to the claims, and thus this Office Action is **NON-FINAL**. Any rejections or objections not reiterated herein from the previous Office Action have been withdrawn in light of the amendments to the claims or as discussed in this Office Action.

This Action is **NON-FINAL**.

Declaration Under 37 CFR 1.132

1. The Declaration of Yuan-Tsong Chen under 37 CFR 1.132 filed 12/07/2007 is sufficient to overcome, in part, the rejection of claims 1 and 8-12 based upon a lack of enablement under 35 USC 112 1st ¶.

Withdrawn Claim Rejections - 35 USC § 112 1st ¶ - New Matter

2. The rejection of claims 1, 8-12, 20 and 22-25 under 35 U.S.C. 112, 1st ¶, as failing to comply with the written description requirement, as presented in the previous Office Action of 09/07/2007, is **WITHDRAWN** in light of the amendments to the claims.

New Claim Rejections - 35 USC § 112 2nd ¶ - Indefiniteness

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 8-10 and 20-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 8 is unclear over recitation of the phrases 'the allele' and 'the nucleic acid' because there is no antecedent basis for any 'allele' or any 'nucleic acid' in either claim 8, or claim 1 from which claim 8 depends. **See MPEP 2173.05(e) for guidance or providing proper antecedent basis.** Claim 8 may be made more clear by putting basis for the required term 'allele' in the independent claim, and by removing the term 'the' from the phrase 'the nucleic acid'.

Claims 9 and 10 are unclear over recitation of the phrases 'the allele' and 'the peripheral blood', in each of claims 9 and 10, because there is no antecedent basis for any 'allele' or any 'peripheral blood' in either claim 9 or 10, or claim 1 from which claims 9 and 10 depend. Claims 9 and 10 may be made more clear by putting basis for the required term 'allele' in the independent claim, and by removing the term 'the' from the phrase 'the peripheral blood' in each claim.

Claims 20-25 are unclear over recitation of the phrase 'wherein said presence is used to indicate predisposition for Stevens-Johnson syndrome or toxic epidermal necrolysis in response to carbamazepine', as recited in claim 20. The phrase, while reciting the term 'used' does not set forth any method steps or limitations as to what is

required for the presence of ant genetic marker to be 'used' to indicate the required predisposition. As such the metes and bound of the claims are unclear. The claims may be made more clear if amended to recite a particular method step consistent with the teaching of the specification, for example, 'correlating the presence of the HLA-B*1502 allele in said sample with a predisposition for an adverse drug reaction in said patient'

Claim 22 is unclear in the recitation of the required limitation of 'determining the presence of at least one genetic factor selected from the group consisting of thiopurine methyltransferase and the genes for the long-QT syndrome'. It is unclear what is required to determine the presence of the recited genetic factor, and how determining the presence is related to the method of pharmacogenomic profiling. The claim may be made clearer if the unclear phrase is amended to recite 'analyzing at least one genetic factor selected from the group consisting of thiopurine methyltransferase and genes for long-QT syndrome'.

Claim 23 is unclear over recitation of the phrases 'the allele' and 'the nucleic acid' because there is no antecedent basis for any 'allele' or any 'nucleic acid' in either claim 23, or claim 20 from which claim 23 depends. Claim 23 may be made more clear by putting basis for the required term 'allele' in the independent claim, and by removing the term 'the' from the phrase 'the nucleic acid'.

Claims 24 and 25 are unclear over recitation of the phrases 'the allele', 'the peripheral blood', and 'the patient', in each of claims 24 and 25, because there is no antecedent basis for any 'allele', 'peripheral blood', or 'patient' in either claim 24 or 25,

or claim 20 from which claims 24 and 25 depend. Claims 24 and 25 may be made more clear by putting basis for the required terms 'allele' and 'patient' in the independent claim, and by removing the term 'the' from the phrase 'the peripheral blood' in each claim.

Claim Rejections - 35 USC § 112 1st Scope of Enablement With New Grounds of Rejection

5. Claims 1 and 8-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

> A method for assessing a risk of a human patient for developing an adverse drug reaction in response to a drug, said method comprising:
>
> detecting the presence of an HLA-B*1502 allele in a sample obtained from said patient; and
>
> correlating the presence of the HLA-B*1502 allele in said sample with an increased risk for an adverse drug reaction in said patient in response to a drug, wherein said adverse drug reaction is Stevens-Johnson Syndrome (SJS) or toxic epidermal necrolysis (TEN), and wherein said drug is carbamazepine.

does not reasonably provide enablement for the broadly recited methods where the presence of HLA-B*1502 is detected in any non-patient sample, or the use of any 'equivalent genetic marker'. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Nature of the invention and breadth of the claims

The claims are drawn to methods for assessing in a patient a risk of SJS or TEN in response to a carbamazepine by determining the presence of the HLA-B*1502,

wherein the presence of the allele is indicative of an increased risk for the specified adverse reaction.

The claims encompass the detection of markers in any sample from any source in the assessment of risk in a particular patient.

Claim 11 encompasses the use of any 'equivalent genetic marker', and claim 12, specifies the equivalent genetic marker Cw*0801 (consonant with the election of species).

The nature of the invention requires knowledge of a relationship between HLA-B*1502 or an equivalent genetic marker in any sample and an increased risk of a particular individual patient to develop SJS or TEN in response to a carbamazepine.

Direction provided by the specification and working example

The specification of the instant application teaches an analysis of HLA-B allele genotype and the development of adverse drug reaction.

The specification teaches that there are various types of adverse drug reactions, and broadly defines 'adverse drug reaction' as an undesired or unintended effect of a drug (p.8, ln.1). The specification teaches that drug eruptions may be mild to moderate in nature (macuolpapular rash, erythema mulitforme, urticaria, fixed drug eruption) or more severe (SJS, TEN) (p.4 lns.10-17).

The specification teaches that there is evidence that adverse drug reactions involve MHC-restricted presentation of drug or drug metabolites.

The specification provides an example of a case:control analysis of HLA-B genotypes and adverse drug reactions in patients. The specification teaches that the

'cases' were 238 individuals with ADRs, wherein 112 patients were diagnosed with SJS/TEN adverse drug reactions (defining this adverse drug reactions as: SJS is skin detachment of less than 10% of body-surface area; overlap SJS-TEN as 10-30%; TEN as greater than 30%; where SJS, overlap SJS-TEN, and TEN are collectively referred to as SJS/TEN (p. 28, lns 6-15), and 126 individuals had milder reactions to various drugs (p.30 – Example 1). Of the 112 SJS/TEN cases, 42 had carbamazepine-induced SJS/TEN (p.28 ln.6). Controls for the analysis provided in the example were 73 carbamazepine-tolerant patients, and 94 non-patients from the general population (p.28 lns.16-21).

The specification teaches the genotyping of subjects' HLA alleles using PCR amplification with sequence specific oligonucleotides and hybridization of the amplification product to a lineblot (p.28 lns.24-30).

The specification provides an analysis of HLA alleles present in patients with carbamazepine–induced SJS/TEN as compared to patients with milder reactions, the general population, and carbamazepine-tolerant patients (Table 1; p.30 ln.29 – p.31 ln.16). The specification teaches that HLA*B-1502 was detected in 42 of 42 SJS/TEN patients who received carbamazepine, but found only in 3 of 73 carbamazepine tolerant patients, 9 of 142 patients with mild adverse reactions, and 5 of 94 general population subjects. The results indicate that the HLA*B-1502 allele is related to carbamazepine–induced SJS/TEN in a statistically significant fashion (Table 1).

The specification teaches that 38 of the 42 carbamazepine-induced SJS/TEN patients also had the HLA-Cw*0801 allele, and that 10 of the 73 carbamazepine-tolerant

subjects had the HLA-Cw*0801 allele. The specification does not provide any statistical analysis of the association of HLA-Cw*0801 with carbamazepine-induced SJS/TEN, nor any analysis of linkage between HLA-B*1502 and HLA-Cw*0801.

State of the art, level of skill in the art, and level of unpredictability

Because the claims generically encompass 'equivalent genetic markers' as well as the specific 'equivalent' genetic marker Cw*0801 for which no statistical analysis regarding any association with SJS or TEN in response to carbamazepine has been provided, it is relevant to point out that the prior art of Thisted (1998) provides guidance as to what is required to indicate that an association is statistically significant. Thisted teaches that it has become scientific convention to say that a p-value of 0.05 is considered significant (p.5 - What does it mean to be 'statistically significant'), and that values above the conventional reference point of 0.05 would not be considered strong enough for the basis of a conclusion.

It is unpredictable as to what markers would be 'equivalent genetic markers' suitable for adverse drug reaction assessment, and whether or not the presence of any 'equivalent genetic marker' (as generically encompassed by the claims) is useful for determining the presence of the HLA-B*1502 allele or for the assessment of risk of drug adverse reaction. While the specification teaches that 38 of 42 (90%) carbamazepine-induced SJS/TEN patients had an HLA-Cw*0801 allele, there is no statistical analysis of the significance of the association of HLA-Cw*0801 with carbamazepine-induced SJS/TEN, nor any analysis of the linkage of HLA-B*1502 with HLA-Cw*0801. Given that (as expressed in Table 5) the HLA-Cw*0801 allele was found in 13.7% of

carbamazepine tolerant individuals and 10.6% of the general population, without any specific analysis of the significance of the association it is not predictable if the presence of the HLA-Cw*0801 allele is a reliable indicator of carbamazepine-induced SJS or TEN. Regarding the linkage of HLA-B*1502 with HLA-Cw*0801, Deng et al (2001) teaches that the traditional criteria are that a Logarithm-of -Odds (LOD) score of > 3.0 is taken as evidence for a significant linkage, a LOD score < -2.0 is taken as evidence against linkage, and a LOD score between -2.0 and 3.0 is not conclusive concerning linkage and exclusion for the genomic region under test (p.314, first full paragraph).

Quantity of experimentation required

A large and prohibitive amount of experimentation would have to be performed in order to use the inventions in the full scope of the claims. One would have to establish, as encompassed by the claims, the merely detecting the presence of HLA-B*1502 in any sample from any source is indicative of an increase risk of an adverse drug reaction in a particular patient (i.e. claims do not require that HLA-B*1502 is detected in a sample derived from the patient). One would also have to determine genetic markers that are 'equivalent' to HLA-B*1502 in any individual, and also establish that any 'equivalent genetic marker' can be used to reliably predict SJS or TEN in response to carbamazepine.

Conclusion

Taking into consideration the factors outlined above, including the nature of the invention and breadth of the claims, the state of the art, the level of skill in the art and its

high level of unpredictability, the lack of guidance by the applicant and the paucity of working examples, it is the conclusion that an undue amount of experimentation would be required to make and use the invention in the full scope in which it is claimed.

Response to Remarks

6. Applicants have traversed (p.6-11 of Remarks) the rejection of claims under 35 USC 112 1st ¶ for lack of enablement. Applicants have argued (p.6-8 of the Remarks) that the Declaration provided by Dr. Yuan-Tsong Chen provides experimental data demonstrating that HLA-B*1502 is directly involved in the development of carbamazepine induced SJS/TEN. The Declaration has been considered and is persuasive in the assertion that HLA-B*1502 is involved in the specified adverse drug reaction, and a such the portions of the rejection as pertaining to enablement with non-Asian patients has been withdrawn.

Applicants have further argued (p.8 of the Remarks) that claim 1 is amended to require detecting the presence of HLA-B*1502 is indicative specifically of an increased risk of an adverse drug reaction. It is noted that the portions of the rejection pertaining to the breadth of the association of the presence of HLA-B*1502 with any risk (i.e. either increased or decreased) have been withdrawn from the rejection. However, the rejection as set forth in this Office Action indicates the breadth of the claims with regard to the detection of HLA-B*1502 (i.e. the claims do not specify that HLA-B*1502 is detected in a sample from the particular assessed patient) in any sample and the assessment of risk of an adverse drug reaction in a particular human patient. The

examiner believes that the claim language provided at the beginning of the rejection would alleviate this portion of the rejection.

Applicants have further argued (p.8-11 of the Remarks) that the specification is enabling for the use of 'equivalent genetic markers'. The arguments assert that the claims (i.e. claims 11 and 12) require a method where: (1) the presence of an equivalent genetic marker is indicative of the presence of HLA-B*1502; and (2) the presence of HLA-B*1502 is indicative of increased risk of the adverse drug reaction (flowchart on page 9 of the Remarks). At issue with the rejection of the claims for lack of enablement in using 'equivalent genetic markers' is the first step in the asserted method, where a marker is required to be indicative of the presence of HLA-B*1502. While Applicants argue that the linkage between, for example, HLA-B*1502 and HLA-Cw*0801 is described in Exhibits submitted with a previous reply, those Exhibits do not indicate a linkage between the two markers such that detecting HLA-Cw*0801 is equivalent to detection HLA-B*1502 in a method of assessing risk of and adverse drug reaction. For example, Table 3 of previously submitted Hung et al shows that while in patients with HLA-B*1502, 59 developed an adverse drug reaction and only 6 were drug tolerant, in analysis of the different marker HLA-Cw*0801 56 developed an adverse drug reaction and 20 were drug tolerant. Thus even the specific marker HLA-Cw*0801 is not 'equivalent' to HLA-B*1502, and is differently associated with risk of adverse drug reaction. That HLA-Cw*0801 is not 'equivalent' to HLA-B*1502 is further exemplified by Table 2 of Hoa et al (2007) and Table 2 of Saito et al (2000), each of which demonstrates that HLA-Cw*0801 is found in haplotypes with HLA-B alleles other than

HLA-B*1502. As such, the rejection as it pertains to the use of any 'equivalent genetic markers' is maintained.

Finally, Applicants have argued (p.10-11 of Remarks) that the genetic factors recited in claim 22 are not required to be associated with CBZ-induced SJS/TEN. It is noted that the portion of the rejection regarding claim 22 is withdrawn in light of the argument.

The rejection as set forth in this Office Action is **MAINTAINED**.

Claim Rejections - 35 USC § 102
Reinstated, as set forth in the Office Action of 5/17/2006

7. Claims 20, 23, and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Trachtenberg (US Patent 5,550,039, Aug. 27, 1996).

Trachtenberg teaches methods for the analysis of HLA-B genotypes using PCR amplification (col.2 lns.37-59) and hybridization of the amplified product to a set of sequence –specific oligonucleotide probes (col.12 lns.38-42).

Regarding claim 20, Trachtenberg teaches a method comprising the same step as required by the claim. The reference teaches determining the presence of HLA-B alleles in a sample (col. 16 – Example 2). The data presented indicates that the presence of several different HLA-B alleles is determined, including HLA-B*1502 and HLA-B*5801 (Table 7).

Regarding claim 23, Trachtenberg teaches using sequence-specific oligonucleotides to determine HLA-B alleles (col.17 lns.4-6), which are oligonucleotides that specifically hybridize with the nucleic acid coding for the allele.

Regarding claim 25, Trachtenberg teaches the use of RNA (col.11 lns.12-17).

Response to Remarks

The rejection of claims under 35 USC 102 as set forth above was presented in the Office Action of 5/17/2006. The rejection was withdrawn in the Office Action of 12/18/2006 in light of the amendments to the claims and arguments presented 09/18/2006. However, in further examination of the claims as presented, the Examiner is reinstating the rejection, and the arguments of 09/18/2006 are addressed here.

Applicants have traversed the rejection of claims under 35 USC 102 as anticipated by the prior art of Trachtenberg. Applicants argue (p.12 of the Remarks of 09/18/2006) that the amended claims require that the presence of HLA-B*1502 is determined, and that 'said presence is used to indicate predisposition for adverse reactions to drugs'. Applicants argue that Trachtenberg does not disclose or suggest that any gene or allele can be used to indicate predisposition for adverse reactions to drugs, and thus Trachtenberg does not teach all of the limitations of independent claim 20. This argument is not found to be persuasive. In a review of the limitations of the claimed method, recitation of the phrase 'used to indicate predisposition for Stevens-Johnson syndrome or toxic epidermal necrolysis in response to carbamazepine' is not presented as a method step, but appears to be merely a recitation of an intended use of the recited single method step of 'determining the presence of HLA-B*1502. This is supported by the fact that the recited 'wherein' clause is not directly related to the purpose of the claimed method as recited in the preamble of the claim. The claim may

be distinguished form the cited prior art if amended to recite a specific method step consistent with the teaching of the specification, for example:

> A method of pharmacogenomics profiling to establish that a human patient is predisposed to developing an adverse drug reaction in response to a drug, said method comprising:
>
> detecting the presence of an HLA-B* 1502 allele in a sample obtained from said patient; and,
>
> correlating the presence of the HLA-B*1502 allele in said sample with a predisposition for an adverse drug reaction in said patient in response to a drug, wherein said adverse drug reaction is Stevens-Johnson Syndrome (SJS) or toxic epidermal necrolysis (TEN), and wherein said drug is carbamazepine.

The rejection as set forth is **MAINTAINED.**

Claim Rejections - 35 USC § 103

8. Claims 22 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Trachtenberg (US Patent 5,550,039, Aug. 27, 1996) in view of Yates et al (1997) as cited in the IDS.

Trachtenberg teaches methods for the analysis of HLA-B genotypes using PCR amplification (col.2 lns.37-59) and hybridization of the amplified product to a set of sequence –specific oligonucleotide probes (col.12 lns.38-42). The data presented indicates that the presence of several different HLA-B alleles is determined, including HLA-B*1502 and HLA-B*5801 (Table 7).

Trachtenberg does not teach determining the presence of the genetic factor thiopurine methyltransferase, or specifically teach analysis of DNA prepared from peripheral blood.

Regarding claims 22 and 24, Yates et al teaches the analysis of thiopurine S-methyltransferase (TPMT) by PCR analysis of the TPMT gene. The reference teaches determining the presence of the genetic factor by analysis of various nucleotide mutations (p.610 – Detection of TPMT mutations by polymerase chain reaction). Relevant to claim 24, Yates et al teaches using nucleic acids prepared from peripheral blood samples (p.609 – Methods, human patients and determination of phenotypes).

It would have been prima facie obvious to one of skill in the art at the time the invention was made to have modified the HLA-B allele determination methods of Trachtenberg so as to have included the TMPT analysis of Yates et al. One would have been motivated to do so because Yates et al teaches the relevance of TPMT analysis applied to organ transplant recipients (p.609, left col., lns.1-6), and Trachtenberg teaches that HLA-B genotyping can be used for tissue typing (col.1 lns.38-44). It would have also been obvious to use the nucleic acids prepared from peripheral blood (as taught by Yates et al) in the HLA-B determination methods of Trachtenberg. One would have been motivated to use nucleic acids from peripheral blood because Yates et al teaches successful PCR analysis of nucleic acids from such samples (p.611 – Results).

Thus, in view of the prior art, the claimed invention is obvious.

Response to Remarks

Applicants have traversed the rejection of claims under 35 USC 103 as obvious in light of the teachings of Trachtenberg in view of Yates et al. Applicants argue (p.13 of the Remarks of 09/18/2006) that Yates et al does not cure the deficiencies of Trachtenberg et al which are argued in the traversal of the rejection of claims as

anticipated by the teachings of Trachtenberg et al. The teachings of Trachtenberg et al with regard to the limitation that the presence of HLA-B*1502 is 'used to indicate predisposition for Stevens-Johnson syndrome of toxic epidermal necrolysis in response to carbamazepine' has been addressed in the previous Response to Remarks.

The rejection as set forth is maintained.

Conclusion

9. No claim is allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Kapushoc whose telephone number is (571)272-3312. The examiner can normally be reached on Monday through Friday, from 8am until 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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